Armed Forces College of Medicine

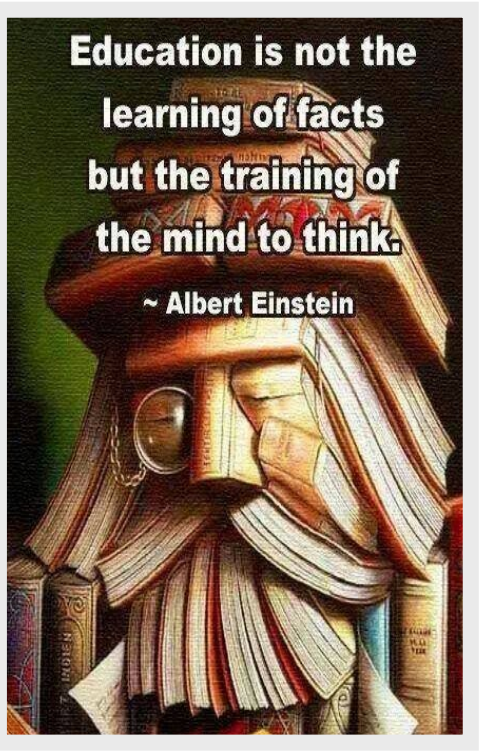
AFCM

Year 2
Endocrine and genitourinary module

Clinical Integrated Cases

Basic Science Principles for Clinical Reasoning

1- Critical thinking
2- Introduction to common forms of disease
3- Apply basic knowledge in a realistic clinical scenario.
4- Interpersonal skills-(share and apply your knowledge)
communication…patient safety
5- Life long self directed learning



Doctor –patient relationship and involving the patients in management decision

Case co-ordinators

Prof. Drs. Manal Hassan, Lamiaa Foad, Nourhan

Sharing Departments

- **Internal medicine**
- **Physiology**
- **Biochemistry**
- **Histology**
- **Pharmacology**

Vomiting with weight loss

Vomiting with weight loss

Mr Magdy is a 14 years old male patient who came to the ER complaining of **severe vomiting and abdominal pain** that started yesterday.

He came into the ER the previous day ,was managed as a case of gastritis and prescribed Proton pump inhibitors, however, he did not improve.

No change in his eating habits during the last week.

On further questioning the patient reported **polyuria and polydepsia** over the last few weeks and **lost a few** kilograms as well.

Vomiting with weight loss

Past History: He has no significant past history of medical illness or surgeries.

No previous drug intake???

Family history irrelevant

Vomiting with weight loss

General examination:

Patient looks extremely ill with marked lethargy.

He has **sunken eyes, dry skin** and mucus membranes.

Vital signs:

Pulse = 97 beats/minute

Blood pressure= 90/60mmHg,

Temp= 36.5°C

Respiratory Rate= 20

He has **rapid deep breathing** , with a **distinctive smell** to his breath.

Discussion

1- a- List the patient problems

b- What is the differential diagnosis?

Problem List

The patient has several problems; from the patient history it is obvious that he has:

1-Abdominal Pain and Vomiting

2-Polyuria and Polydepsia

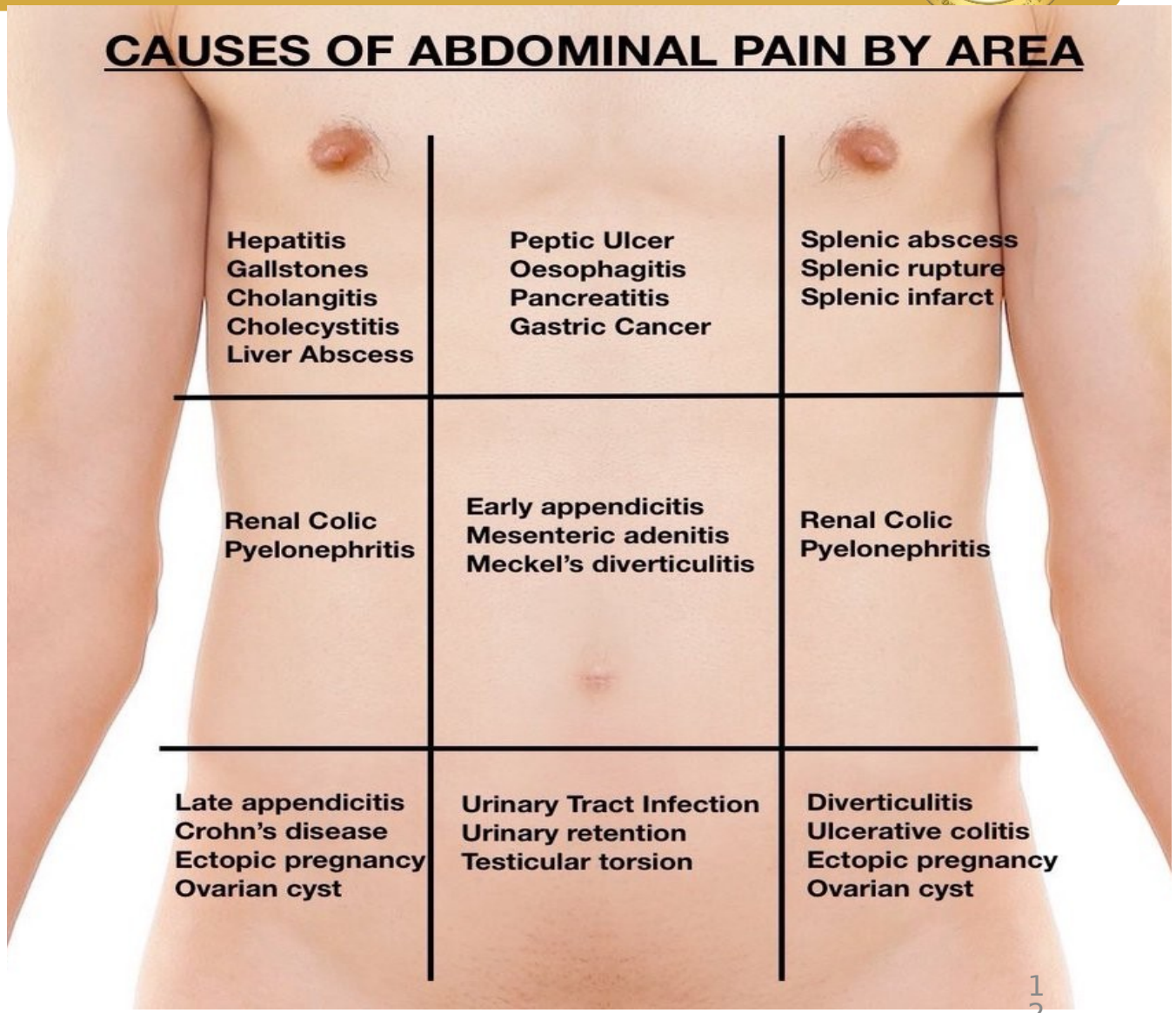
3-Weight Loss

From the patient Examination it is obvious that he has:

4-Dehydration

5-Hyperventilation

If we approach this case as a case of abdominal pain we will have numerous causes



So let’s narrow our DD by approaching this patient as a case of polyuria

Polyuria is defined as urine output exceeding 3L/day

1-Water Diuresis:

- DI either central or nephrogenic (Hypercalcemia,Hypokalemia)
- Psychogenic Polydepsia
- Drugs e.g:Diuretics

2-Solute Diuresis:

- Hyperglycemia (DM)
- Exogenous solute load (sodium Bicarbonate TPN)

2- Explain the polyuria and polydipsia in this patient

✓ **Polyuria** (passage of large volumes of urine)

is due to excretion of osmotically active molecules e.g glucose loss of large amounts of water (osmotic diuresis).

✓ **Polydipsia** (excessive drinking)

Dehydration 2ry to osmotic diuresis activates the mechanisms regulating water intake polydipsia.

N.B :

In DM, lack of insulin leads to hyperglycemia which is manifested by **3Ps** (polyuria, polydipsia & polyphagia).

He has sunken eyes, dry skin and mucus membranes

Explain

Because of hyperglycemia leads to osmotic diuresis which leads to **dehydration**

He has rapid deep breathing ,RR=20 with a distinctive smell to his breath

3- Explain the rapid deep breathing

- ✓ Insulin deficiency and glucagon excess shunts the free fatty acids into ketone body formation.
- ✓ Accumulation of these keto acids results in metabolic acidosis (diabetic ketoacidosis, DKA) and compensatory rapid deep breathing in an attempt to washout excess CO 2 (Kussmaul respiration).

4- What are the investigation that are needed for this patient?

Welcome Back

Vomiting with weight loss

The doctor asked for:
Random Blood Sugar and
Blood Gases

Our patient had a high RBS = 680mg/dl

so the Doctor asked for **urine dipstick testing**

for acetone

Acetone in urine was found to be +++

ABG:
ph= 7.29 (N= 7.35-7.45) **Interpret the investigation resu**
HCO_3= 14 (N= 22-28)

Due to the insulin deficiency and release of large amounts of glucagon, free fatty acids circulate in abundance in the blood and are metabolized into acetoacetic acid and B-hydroxybutric acid - both of which are **strong organic acids and are referred to as ketones.**

An increase in ketone production and a decrease in peripheral cell use lead to **metabolic acidosis**

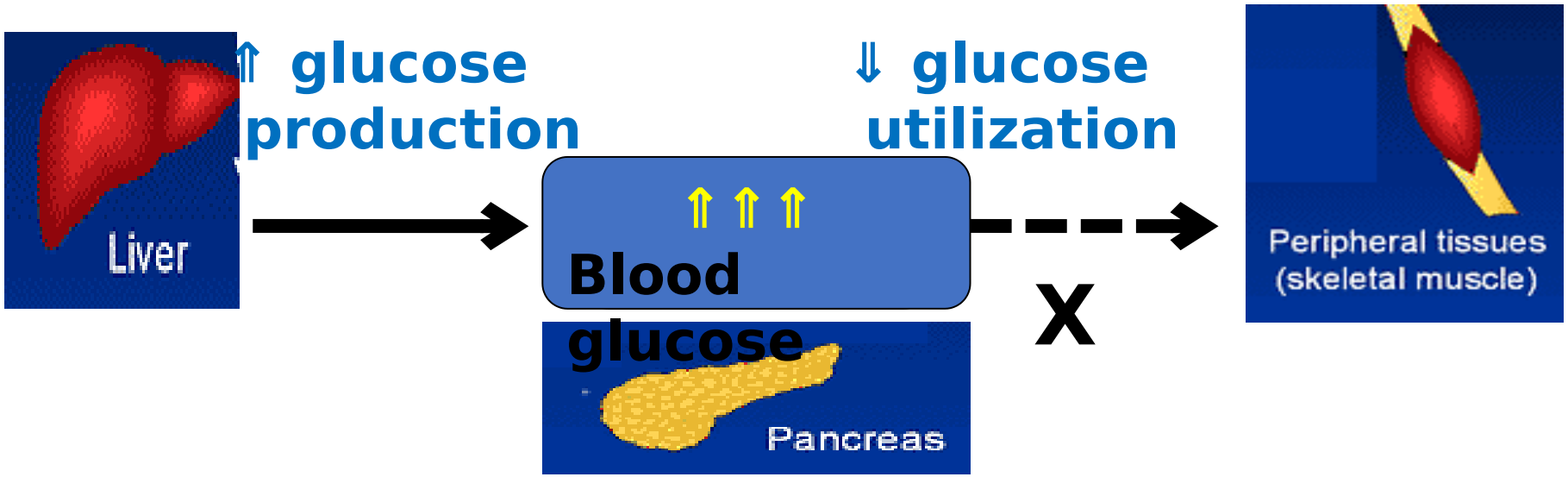
RBS = 680mg/dl

Explain the rise in blood sugar level

Causes of hyperglycemia in DM:

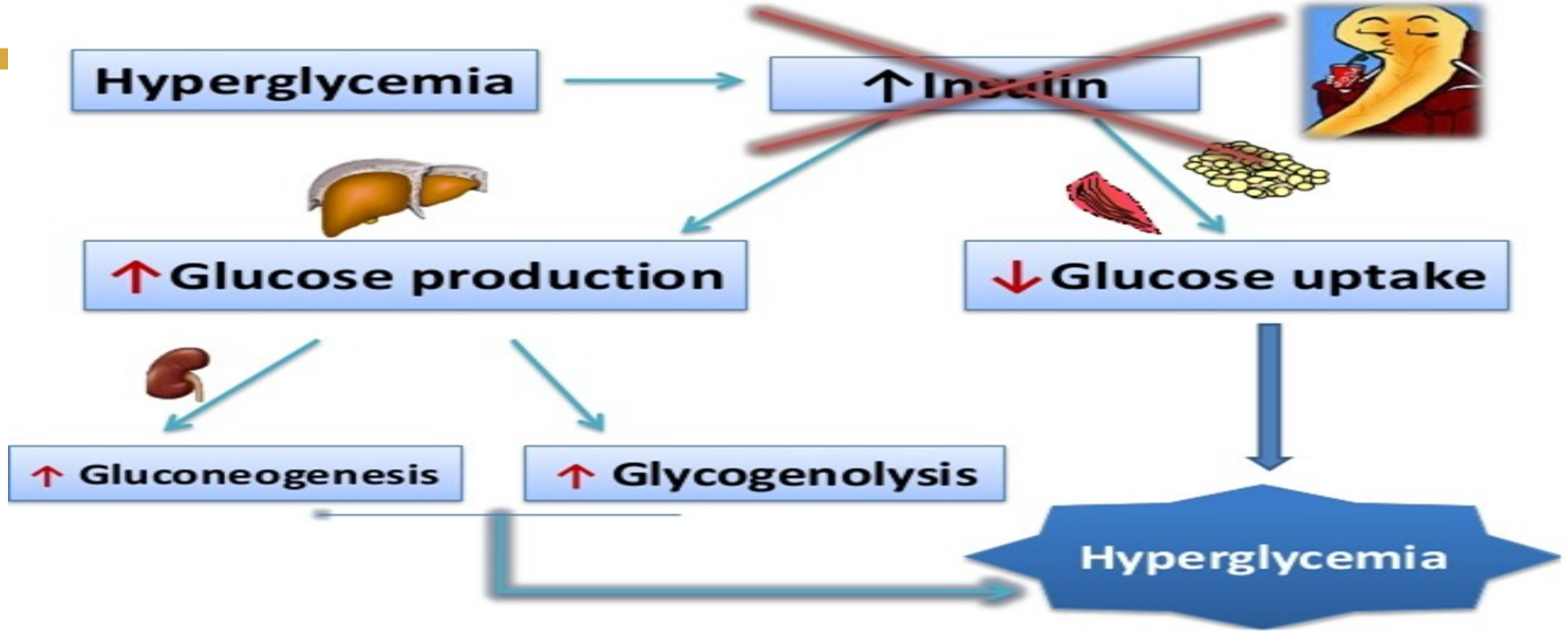
Due to decreased peripheral glucose utilization by cells & increased hepatic glucose output

(extracellular glucose excess + intracellular glucose deficiency)



Impaired insulin secretion or

Causes of hyperglycemia in DM:



I. **Decreased peripheral glucose disposal (uptake) by muscles &adipose tissue due to:** Lack of insulin.

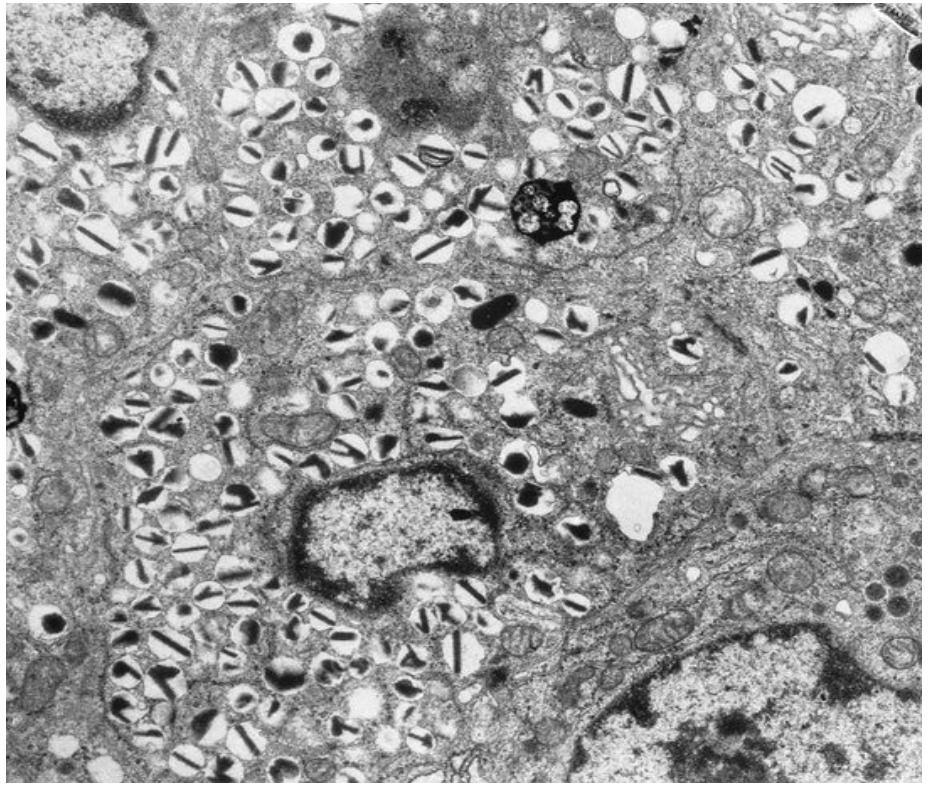
II. Increased hepatic glucose output due to:

1- Enhanced gluconeogensis (↑ lipolysis glycerol & catabolism amino acids)

2- Enhanced glycogenolysis.

5- What is the defective cell in this condition?

Beta cells in the islets of Langerhans



70 %, Situated mainly **centrally**
LM: Relatively **small**
different grades of **basophilia**
EM:Rough endoplasmic reticulum

- Golgi apparatus, numerous secretory granules with dense polyhydral core and a pale matrix. The polyhedral core is believed to be

Acetone in urine was found to be +++

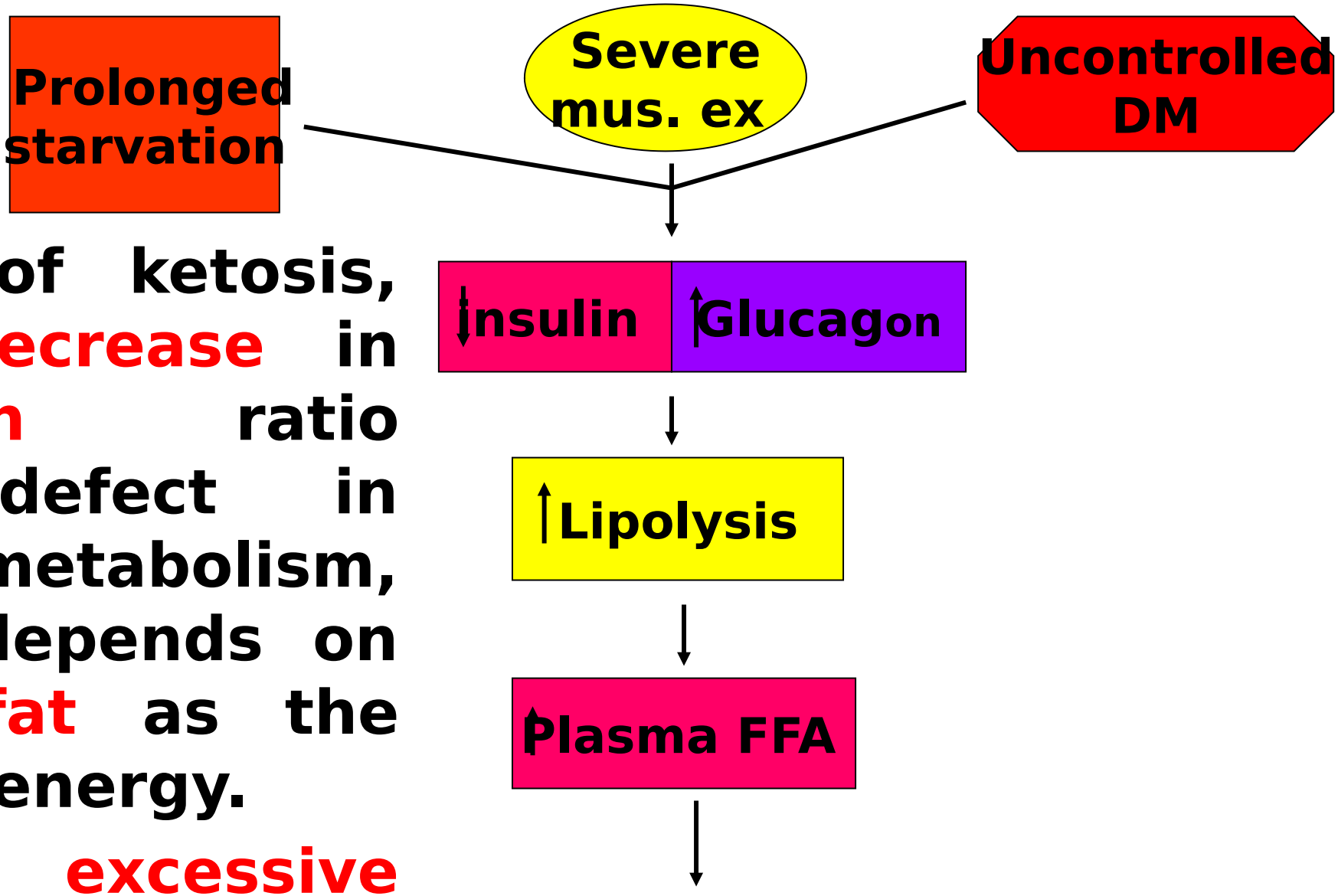
pH=7.29

6- Explain the biochemical basis of this result

Ketone Bodies (KB)

1. *Acetoacetate*
2. *β-hydroxybutyrate*
3. *Acetone.*

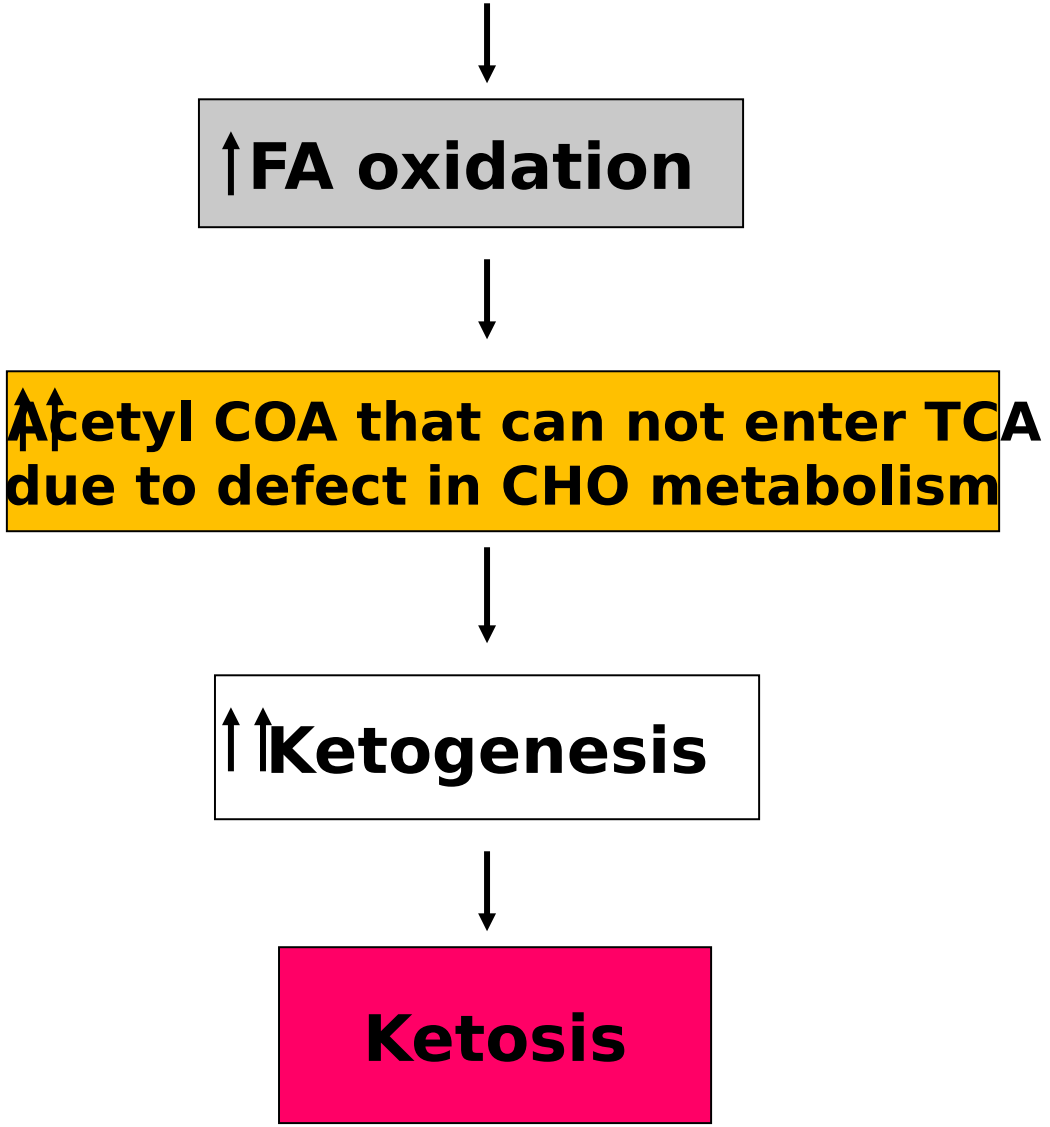
Mechanism of Ketosis:



- In all types of ketosis, there is a **decrease** in **insulin/glucagon** ratio causing a defect in carbohydrate metabolism, so the body depends on **oxidation of fat** as the main source of energy.
- So, there is **excessive lipolysis** in adipose tissue

Mechanism of Ketosis:

- The latter are oxidized to produce large amounts of acetyl COA that can not enter the citric acid cycle due to deficiency of oxaloacetate.
- Consequently, acetyl COA is diverted to the pathway of ketogenesis leading to excessive formation of



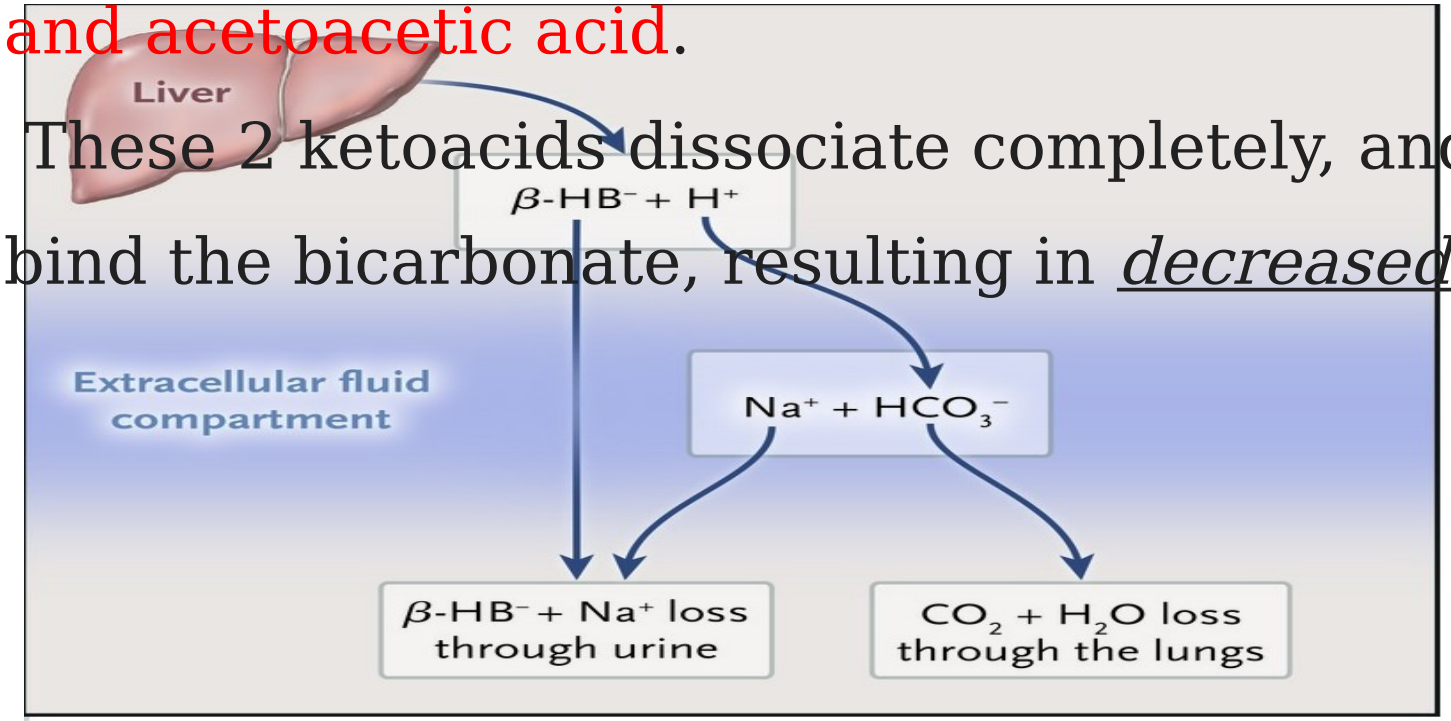
HCO3=14

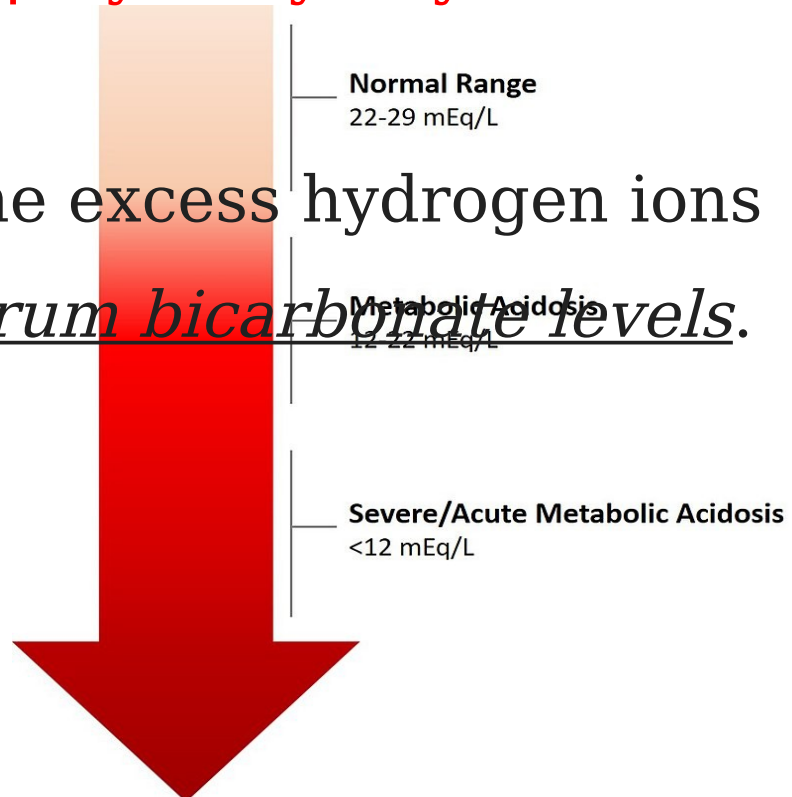
Explain

- ✓ Insulin deficiency → ↑ hepatic glucose production & ↓ glucose uptake → hyperglycemia

→ stimulate lipolysis and ketogenesis, resulting in ketoacidosis.

- ✓ Acidosis in DKA is due to the overproduction of β-hydroxybutyric acid and acetoacetic acid.
- ✓ These 2 ketoacids dissociate completely, and the excess hydrogen ions bind the bicarbonate, resulting in *decreased serum bicarbonate levels*.





Do you need further investigations?

The doctor asked for the following lab investigations

- HbA1C
- Creatinine
- Urea
- Sodium
- Potassium
- CBC

Results:

- HbA1C: 7.7%
- Creatinine:1.5 mg/dl
- Urea:55 mg/dl
- Sodium:135mg/dl
- Potassium:4.5 mg/dl
- CBC:

Hb:15 g/dl TLC:**12,000** Platelets :322,000

o , the doctor asked for **urine analysis, chest x-ray, CRP**

Discussion

7- HbA1C: 7.7%

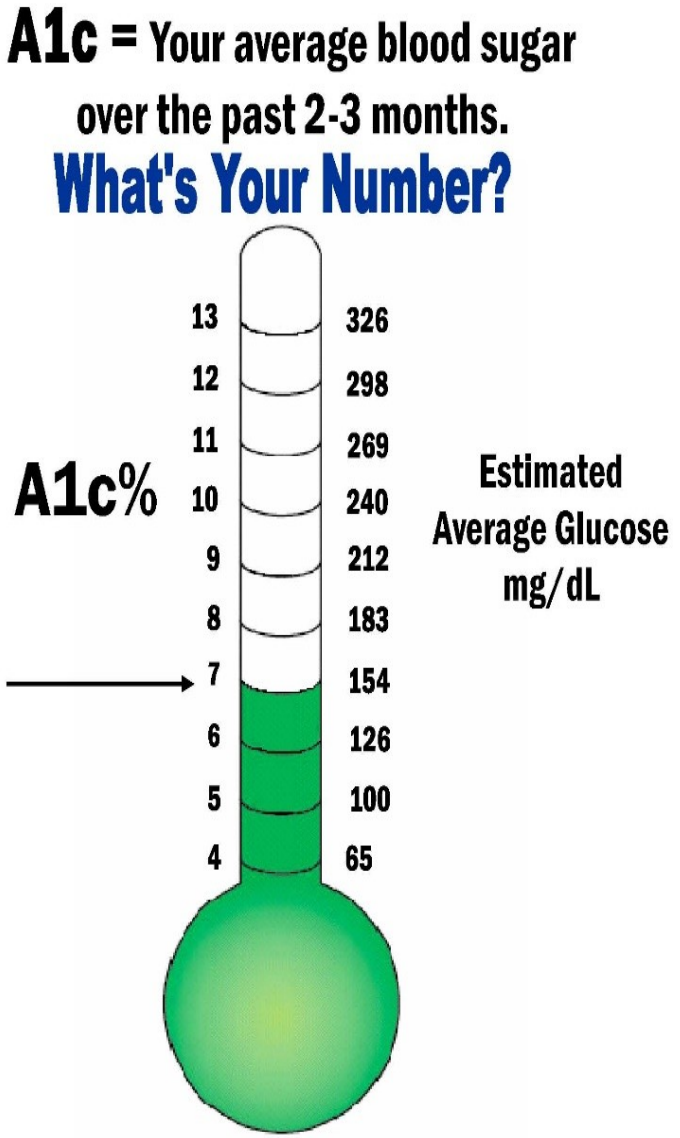
Explain

Glycosylated hemoglobin

Glycosylated hemoglobin is non-enzymatic conjugation of Hg with glucose.

HbA1C is the investigation of choice to monitor therapy as it gives an idea about the blood glucose level over the previous few months.

What is the relation between HbA1C and the blood glucose level?



What is your final diagnosis?

Diagnosis of DM

Assay	Description	Criteria for Diabetes
Hb A_{1C}	Performed in laboratory by method NGSP-certified and standardized to DCCT assay	≥ 6.5 %
Fasting plasma glucose	At least 8 hour fast	≥ 126 mg/dL
Random plasma glucose	In persons with symptoms of hyperglycemia or hyperglycemic crisis: Blood glucose measured at any time of day	≥ 200 mg/dL
Two-hour plasma glucose	Following a glucose load of 75 g anhydrous glucose dissolved in water	≥ 200 mg/dL

Diagnosis

This young patient was presented by polyuria, polydipsia, abdominal pain and weight loss. On examination he showed marked dehydration with acidotic breathing. His labs showed :

high RBS, ketonuria, Metabolic Acidosis, High HbA1c

This all goes with the diagnosis of **Type 1 DM complicated by Diabetic Ketoacidosis**

Table 1. "Five Is" Precipitating Diabetic Ketoacidosis/Hyperosmolar Hyperglycemic State

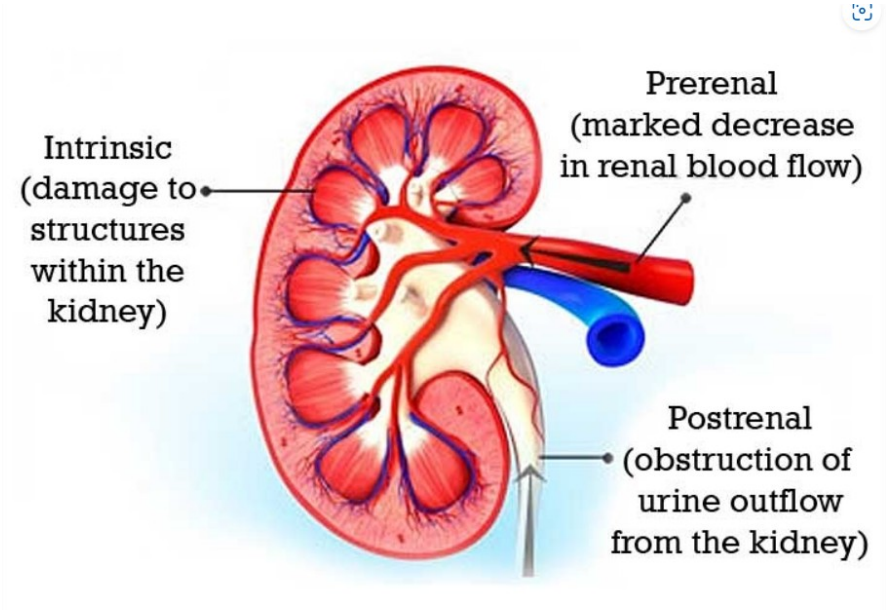
Precipitant	Specific Examples
Infection	Pneumonia, urinary tract infection, skin infections
Infarction	Myocardial infarction, stroke, bowel infarction
Infant on board	Pregnancy
Indiscretion	Dietary noncompliance
Insulin deficiency	Noncompliance with insulin; pump failure

Creatinine:1.5 mg/dl
Urea:55 mg/dl

Explain

Creatinine:1.5 mg/dl
Urea:55 mg/dl

Dehydration is a cause for pre-renal impairment results in increase creatinine and urea levels



Explain glucose transport across body cells

8- What are the type of glucose transporters expected to be defective in this patient?

✓ Glucose transport across the body cells occurs by :

1. **Secondary active transport:** (**Na^+** - glucose cotransport) (SGLT1 & SGLT2) in intestine & kidney.
2. **Facilitated diffusion:** glucose transporters (GLUT).

There are 7 different glucose transporters, named GLUT 1–7.

Typ	characteristics
GLUT 1	Basal glucose uptake (ercs, muscle cells at resting conditions, brain vessels ..)
GLUT 2	Liver, β cells of pancreas , kidney
GLUT 3	Neurons, placental cells
GLUT 4	Muscle, adipocytes – dependent on insulin
GLUT 5	Transport of fructose, small intestine
GLUT 7	Intracelular transport liver

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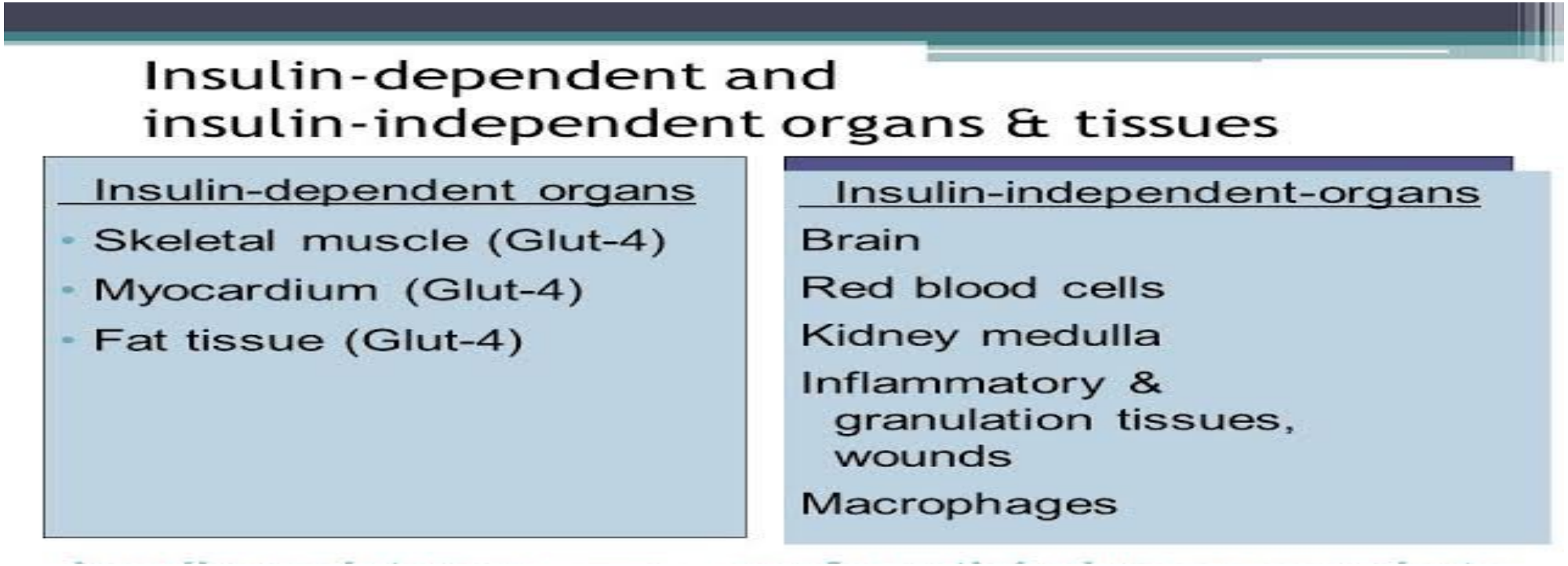
Glucose Transporters



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Explain the loss of weight in this patient.

Weight loss is due to:

- Lack of lipogenic and anabolic action of insulin.
- Glucosuria as for every gram of glucose excreted, 4.1 kcal is lost from the body.

Welcome Back

Vomiting with weight loss

- Patient was admitted to the ICU
- A wide bore canula was inserted into ou
- **fluid resuscitation** was started togeth
- **short acting insulin** infusion at 0.1u/kg/h ,with hourly monitoring of RBS, urine output ,Acetone in urine and venous blood gases/6h.

9- What is the treatment strategy for this patient?

DKA

Management

GOALS

- Fluid resuscitation
- Reversal of the acidosis and ketosis
- Reduction in the plasma glucose concentration
- Replenishment of electrolyte and volume losses
- Identification the underlying cause

PHARMACOTHERAPY

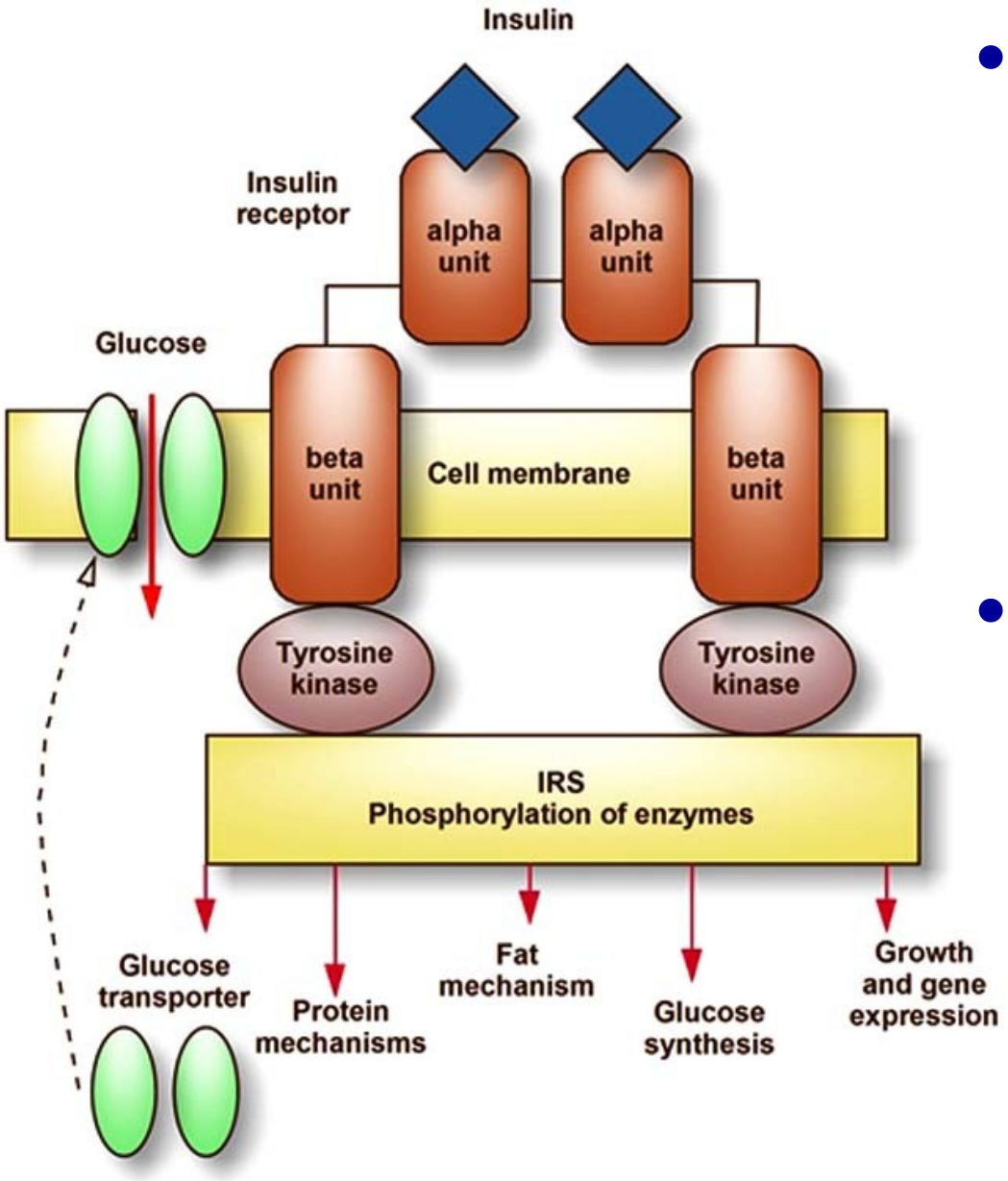
- ❑ Short-acting insulins
- ❑ IV Fluids
- ❑ Electrolyte supplements (e.g. Potassium Chloride)
- ❑ Alkalinizing agents (e.g. Sodium Bicarbonate)
- ❑ Antibiotics

10- What is the short acting insulin preparation suitable for this patient? Explain your choice

The short-acting preparation that is suitable in this patient is:

- **Regular human insulin →→ it could be injected I.V in the emergency as it is clear and soluble and is not a suspension**

What is the mechanism of action of insulin?



- Insulin binds to specific membrane receptors, each receptor has α & β subunits connected together by 2 bisulphide bridges.
- Activation of tyrosine kinase activity → Phosphorylation of intracellular proteins→ Change in enzyme activity, gene expression and translocation of Glut-4 transporter→→→Glucose uptake by adipose tissue &

Illustrate long term insulin regimen plan for that patient after discharge (home management)?

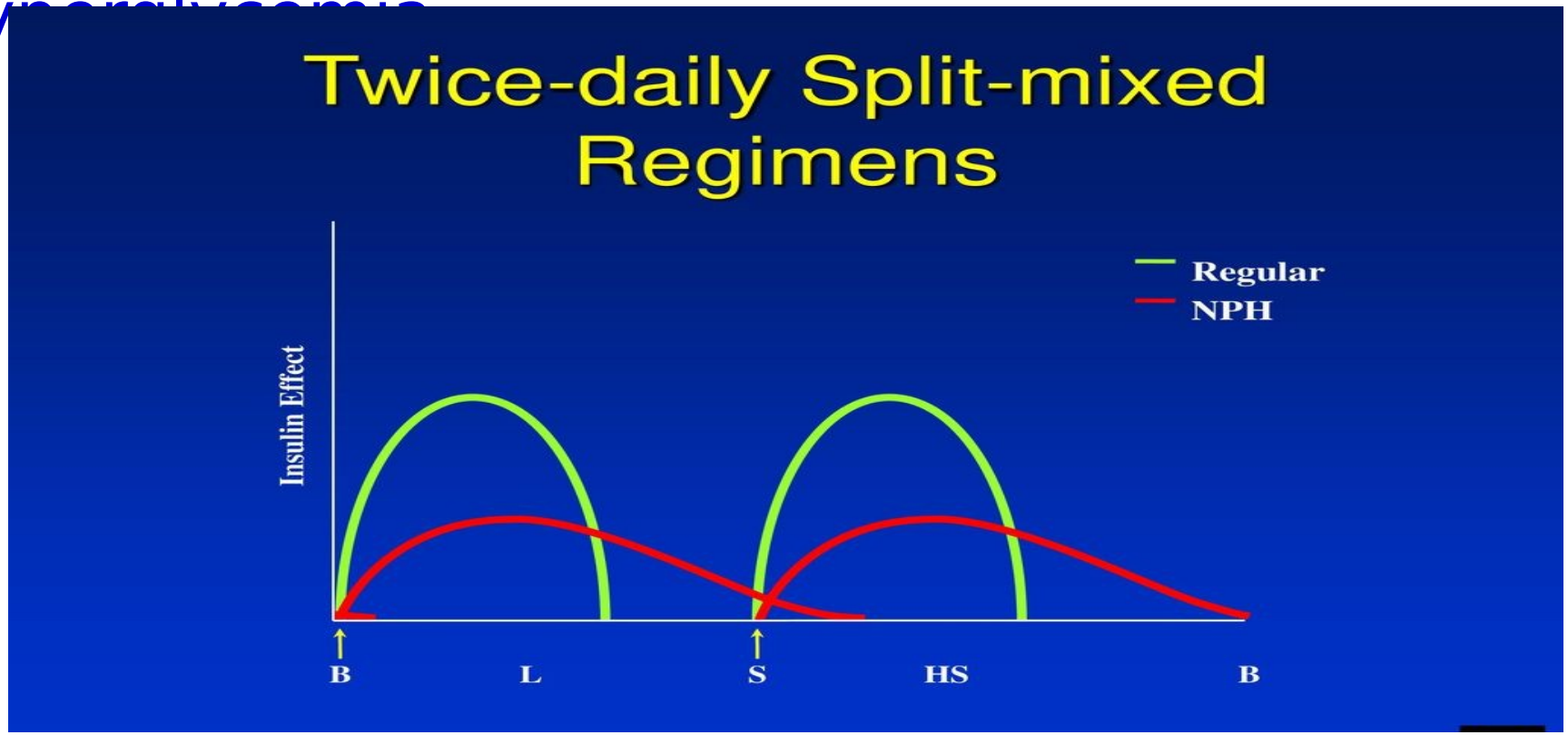
Regimens of insulin therapy that are usually could be used:

A)Split-mixed regimen

B) Basal-bolus insulin regimen (Multiple daily injections)

Regimens of insulin therapy

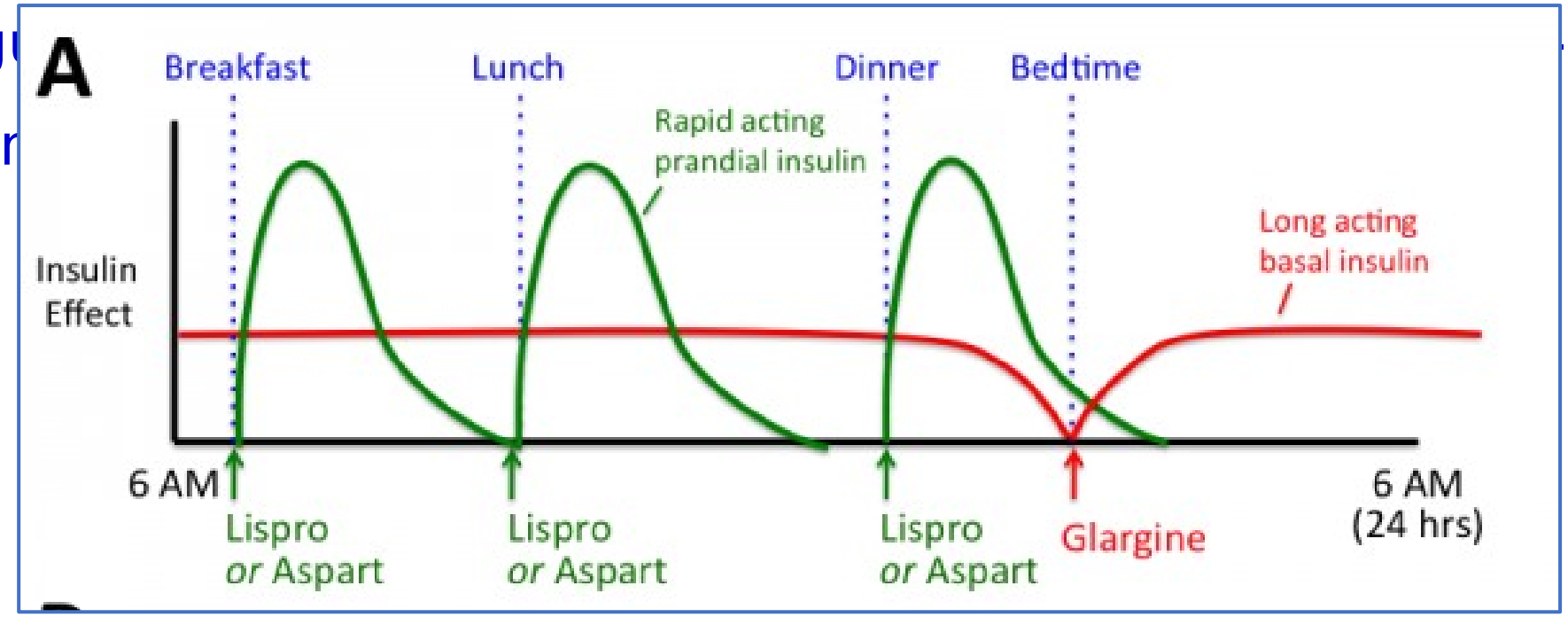
A) Split-mixed regimen: Regular + NPH insulin dose split to 2 parts; 2/3 given 30 min before breakfast, 1/3 before supper to prevent overnight hyperglycemia



B) Basal-bolus insulin regimen (Multiple daily injections):

Insulin glargine or Detemir given once to achieve a more stable basal activity.

Regu
r



11- What are the adverse effects of insulin?

Adverse Effects

1) Hypoglycemia: ttt?

MOST **Serious** & **Common** in an overdose

2) Hypokalemia

3) Lipodystrophy.

4) Insulin resistance .

5) Allergic reactions.

(less common with human insulin)

How would you follow up this patient?

Follow Up

Our Patient requires :

1-Regular Fup of his blood glucose **(FBS, post prandial)**

2-**HbA1c:**every 3 months for long term control

3-Screening for **microvascular complications** (After 5 years in type 1 patients)

a-Nephropathy:

- At least annually, urinary albumin (e.g., spot urinary albumin-to-creatinine ratio) and estimated glomerular filtration rate should be assessed in people with type 1 diabetes with duration of ≥5 years

b-Retinopathy: Adults with type 1 diabetes should have an initial dilated and comprehensive eye examination within 5 years after the onset of diabetes

c-Neuropathy: All people with diabetes should be assessed for diabetic peripheral neuropathy starting at 5 years after the diagnosis of type 1 diabetes and at least annually thereafter.

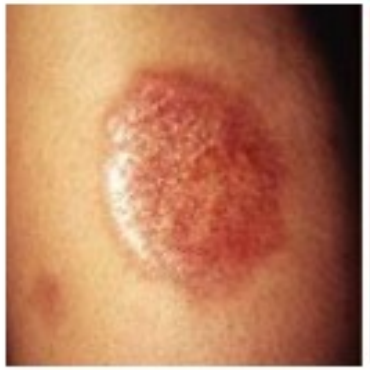
Take home message

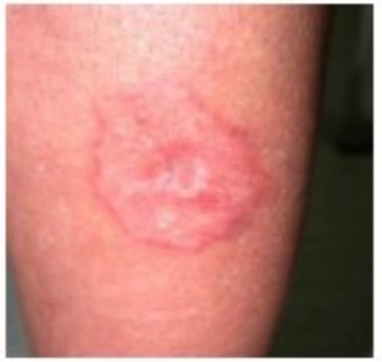
- Diabetic keto-acidosis (DKA) is the most serious complication of type 1 diabetes.
- The most important presentation of DKA is dehydration, vomiting, abdominal pain, kussmaul breathing, metabolic acidosis, ketosis and Disturbed level of consciousness.
- Common precipitating factors for DKA are infections, infarction and missed insulin dose.


Thank
you

(e.g. 45 year old male presented with polyurea, polydipsia, poly phagia, Fasting bl glucose levels on two occasions >150 mg%.)

On Examination





Body Weight: - 70kg
Blood Pressure: - 140/90
WBC: -
PLT: - 150
Hb: - 13g/L
Fasting Blood Sugar: - 170mg%
Fasting Cholesterol:-270mg%
Hb A1c:- 13.7 %

Laboratory Results from PCP appointment:

Pertinent Normals and Abnormals:

- Fasting serum glucose - 251 mg/dL (hig
- HbA1c - 13.7% (high)
- BUN - 12 mg/dL (normal)
- Creatinine - 1.1 mg/dL (normal)
- CO2 - 20mEq/L (low)
- Anion gap - 13 mEq/L (normal)
- TSH - 2.72 IU/L (normal)

In-office Lab from First Appointment with Diabetes Spe Team:

- Dipstick Urinalysis:
  - Specific gravity – 1.030 (normal
  - Ketones – 4+ (high)
  - Glucose – 2000+ (high)
  - Protein – small amount (abnorma
- Random fingerstick glucose – 395 mg/dL (h